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L3 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:893456 HCAPLUS
DOCUMENT NUMBER: 136:177615
TITLE: Phosphotyrosyl peptides block Stat3-mediated DNA binding activity, gene regulation, and cell transformation
AUTHOR(S): Turkson, James; Ryan, Declan; Kim, Joon S.; Zhang, Yi; Chen, Zhi; Haura, Eric; Laudano, Andy; Sebti, Said; Hamilton, Andrew D.; Jove, Richard
CORPORATE SOURCE: Molecular Oncology, H. Lee Moffitt Cancer Center and Research Institute, the Departments of Oncology, University of South Florida College of Medicine, Tampa, FL, 33612, USA
SOURCE: Journal of Biological Chemistry (2001), 276(48), 45443-45455
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Signal transducers and activators of transcription (STATs) comprise a family of cytoplasmic signaling proteins that participates in normal cellular responses to cytokines and growth factors. Frequently, however, constitutive activation of certain STAT family members, particularly Stat3, has accompanied a wide variety of human malignancies. To identify small mol. inhibitors of Stat3, we investigated the ability of the Stat3 SH2 domain-binding peptide, PY*LKTK (where Y* represents phosphotyrosine), to disrupt Stat3 activity in vitro. The presence of PY*LKTK, but not PYLKTK or PFLKTK, in nuclear exts. results in significant redn. in the levels of DNA binding activities of Stat3, to a lesser extent of Stat1, and with no effect on that of Stat5. Analyses of alanine scanning mutagenesis and deletion derivs. of PY*LKTK reveal that the Leu residue at the Y + 1 position and a substituent at the Y - 1 position (but not necessarily Pro) are essential for the disruption of active Stat3, thereby mapping the min. active sequence to the tripeptide, XY*L. Studies involving bead-coupled PY*LKTK peptide demonstrate that this phosphopeptide directly complexes with Stat3 monomers in vitro, suggesting that PY*LKTK disrupts Stat3:Stat3 dimers. As evidence for the functional importance of peptide-directed inhibition of Stat3, PY*LKTK-mts (mts, membrane translocating sequence) selectively inhibits constitutive and ligand-induced Stat3 activation in vivo. Furthermore, PY*LKTK-mts suppresses transformation by the Src oncoprotein, which has been shown previously to require constitutive Stat3 activation. Altogether, we have identified a minimal peptide that inhibits Stat3 signaling and provides the conceptual basis for use of this peptide as a lead for novel peptidomimetic drug design.

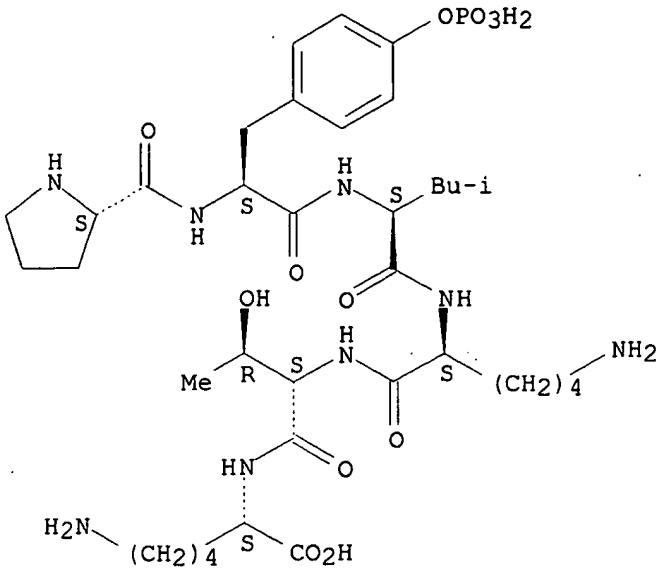
IT **286465-26-7 286465-27-8 286465-38-1 286465-39-2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphotyrosyl peptides block Stat3-mediated DNA binding activity, gene regulation, and cell transformation)

RN 286465-26-7 HCAPLUS
CN L-Lysine, L-prolyl-O-phosphono-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 PYLKTK

Absolute stereochemistry.

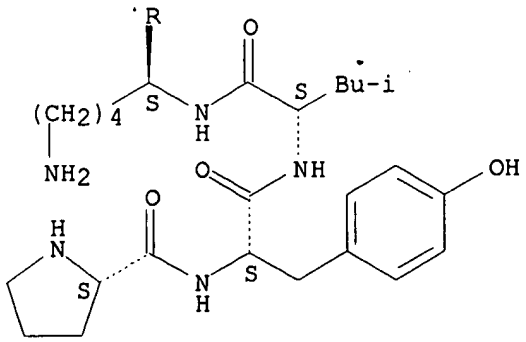


RN 286465-27-8 HCAPLUS
CN L-Lysine, L-prolyl-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

SEQ 1 PYLKTK

Absolute stereochemistry.

PAGE 1-A



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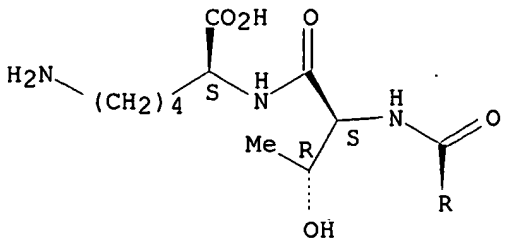
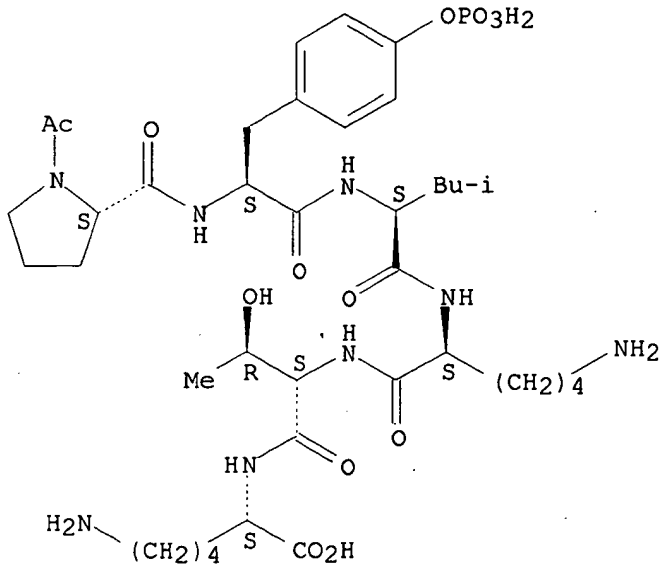


RN 286465-38-1 HCAPLUS
CN L-Lysine, 1-acetyl-L-prolyl-O-phosphono-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

NTE modified

SEQ 1 PYLKTK

Absolute stereochemistry.



RN 286465-39-2 HCAPLUS
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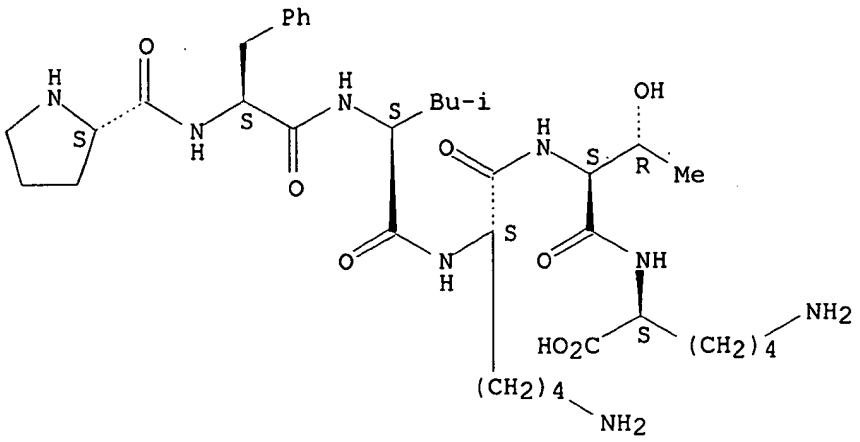
SEQ 1 PFLKTK

Absolute stereochemistry.



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:763492 HCAPLUS
DOCUMENT NUMBER: 135:315574
TITLE: Methods for the detection of modified peptides, proteins and other molecules
INVENTOR(S): Volinia, Stefano
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001031469	A1	20011018	US 2001-753114	20010102

PRIORITY APPLN. INFO.: US 2000-174171P P 20000103

AB A method is described for the mol. anal. of complex samples, including biopsies from cancer and other multifactorial diseases. The method uses arrays of proteins and enzymes substrates, including peptides, antibodies, non peptide substrates and phospho-protein and acetyl-protein traps. In an embodiment, tagged substrates are mass reacted in soln. with the sample under investigation and then sorted onto a solid surface array by means of the relative tags. In another embodiment the substrates are immobilized onto a solid surface prior to sample anal.

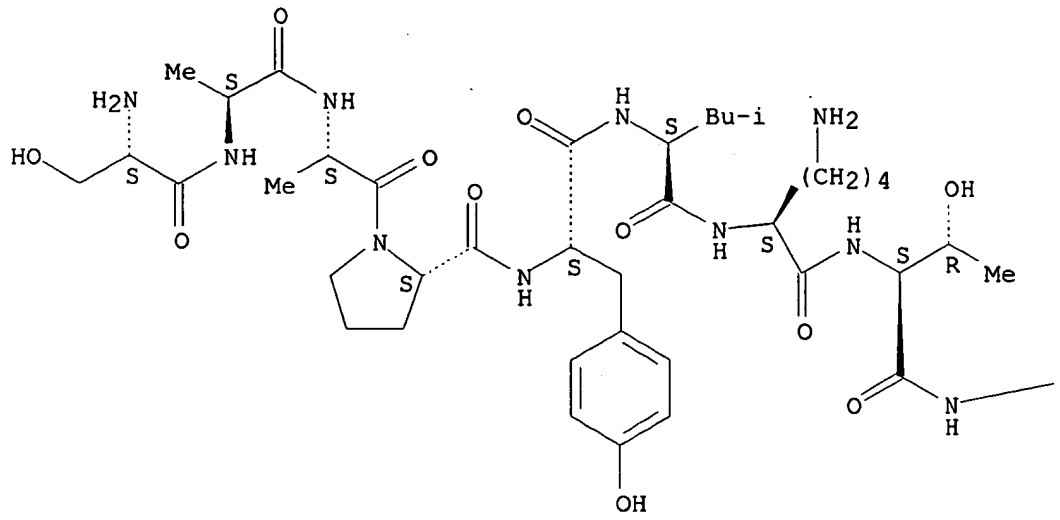
IT **367451-89-6D**, conjugates with oligonucleotide complementary to tag in array
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(methods for detection of modified peptides and proteins and other mols.)

RN 367451-89-6 HCAPLUS

CN L-Lysine, L-seryl-L-alanyl-L-alanyl-L-prolyl-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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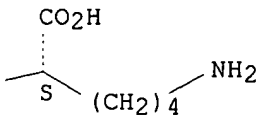


IT **367451-81-8P 367451-89-6P**
RL: ARG (Analytical reagent use); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(methods for detection of modified peptides and proteins and other mols.)

RN 367451-81-8 HCAPLUS

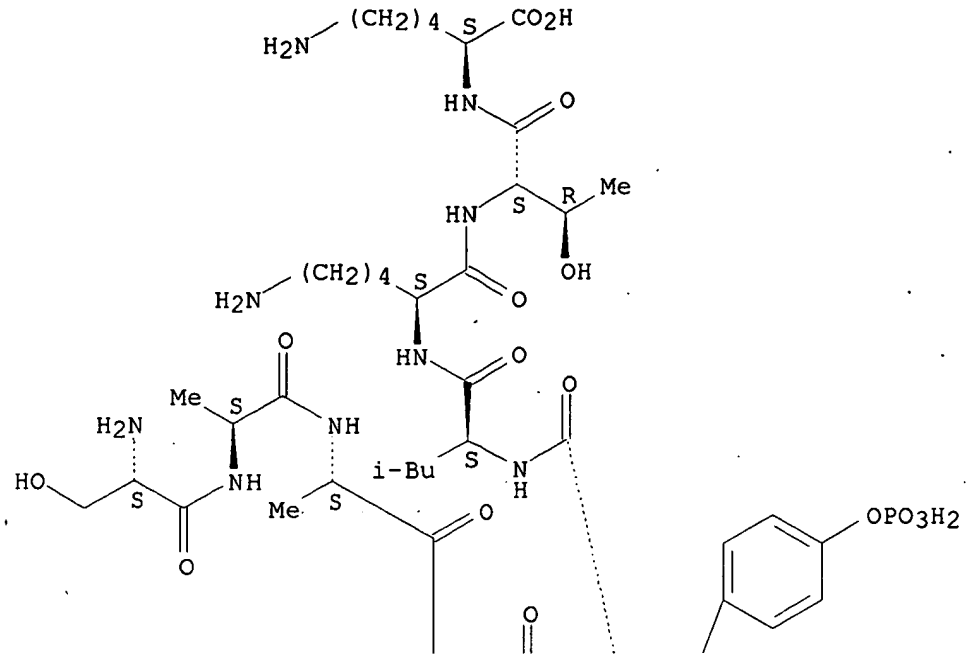
CN L-Lysine, L-seryl-L-alanyl-L-alanyl-L-prolyl-O-phosphono-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 SAAPYLKTK

Absolute stereochemistry.

PAGE 1-A



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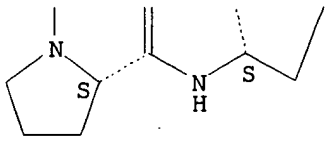
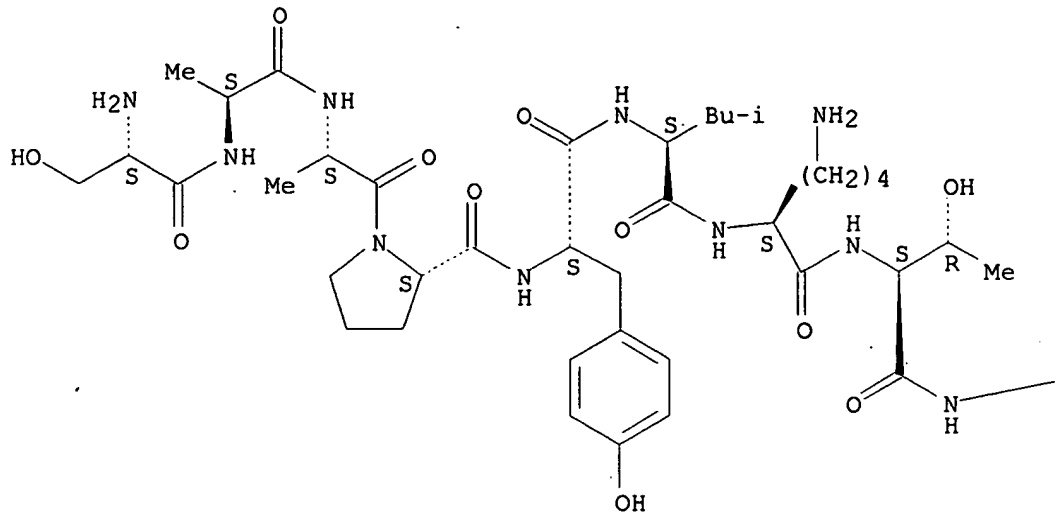


RN 367451-89-6 HCAPLUS
CN L-Lysine, L-seryl-L-alanyl-L-alanyl-L-prolyl-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

SEQ 1 SAAPYLKTK

Absolute stereochemistry.

PAGE 1-A



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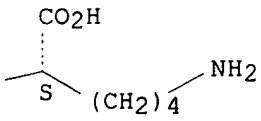

L3 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:535166 HCAPLUS
DOCUMENT NUMBER: 133:129859
TITLE: Inhibition of STAT3 signal transduction and the treatment of cancer in humans
INVENTOR(S): Jove, Richard; Dalton, William; Sebti, Said; Yu, Hua; Heller, Richard; Jaroszeski, Mark
PATENT ASSIGNEE(S): University of South Florida, USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044774	A2	20000803	WO 2000-US1845	20000127
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1146869	A2	20011024	EP 2000-905724	20000127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-117600P P 19990127
WO 2000-US1845 W 20000127

AB Signal Transducer and Activator of Transcription (STAT) proteins have a fundamental role cell signaling, and are activated by a large no. of cytokines and growth factors. One member of the STAT family, STAT3, has a crit. role in oncogenesis. The present invention relates generally to disruption of the pathway of STAT3 signaling in the treatment of human cancer. STAT3 activation is shown to be present in diverse tumor cell lines and tumors, to promote oncogenesis, to inhibit apoptosis, and to reduce sensitivity to chemotherapeutic agents. Inhibition of STAT3 signaling induces apoptosis specifically in tumor cell lines, and increases sensitivity to chemotherapeutic agents. The invention relates more particularly to methods, compns., means of administering such compns., and means for identifying such compns. for the inhibition of STAT3 intracellular signaling in the treatment of human cancers. Activation of STAT3, as measured EMSA, was inhibted in tumor cell lines by inhibitors of Src and Jak protein tyrosine kinases. The Jak kinase inhibitor AG490 blocked the proliferation of human mammary tumors in nude mice. Blocking of serine phosphorylation of STAT3 had similar effects.

IT **286465-26-7 286465-27-8 286465-38-1**
286465-39-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ligand for STAT3; inhibition of STAT3 signal transduction and treatment of cancer in humans)

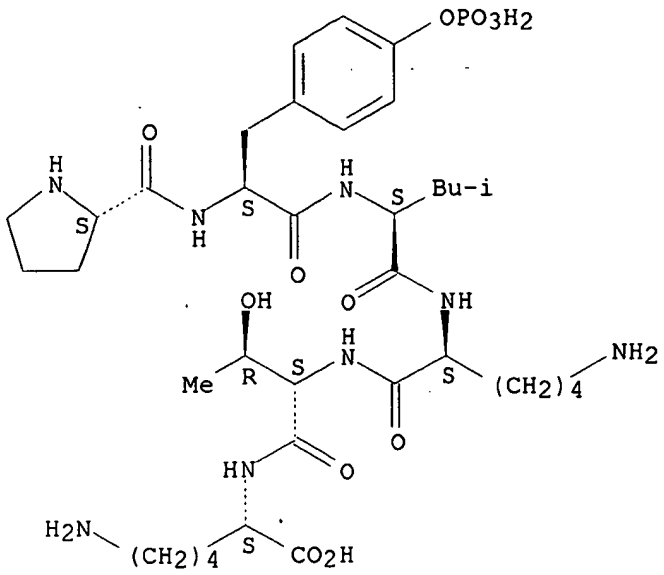
RN 286465-26-7 HCAPLUS

CN L-Lysine, L-prolyl-O-phosphono-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 PYLKTK

Absolute stereochemistry.

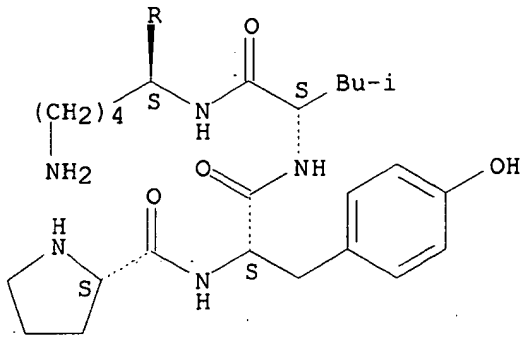


RN 286465-27-8 HCAPLUS
CN L-Lysine, L-prolyl-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

SEQ 1 PYLKTK

Absolute stereochemistry.

PAGE 1-A



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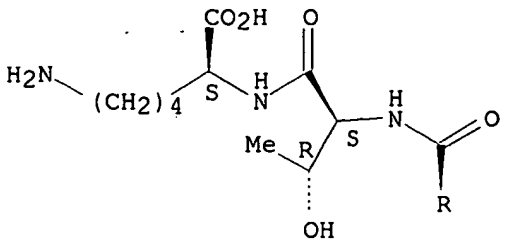
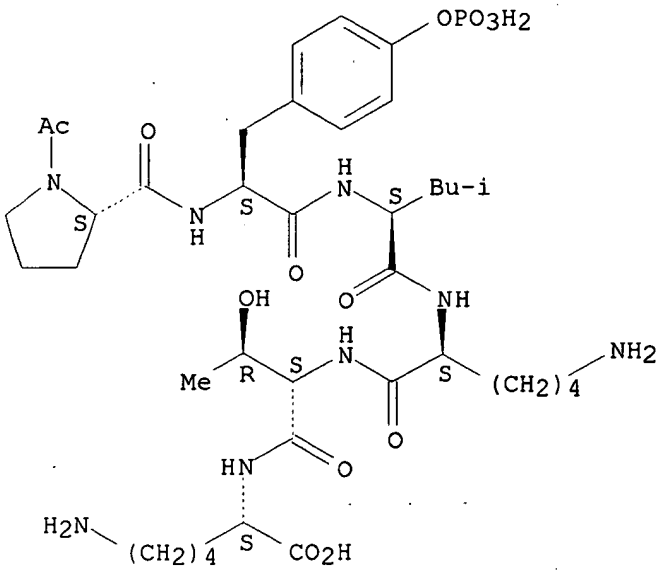


RN 286465-38-1 HCAPLUS
CN L-Lysine, 1-acetyl-L-prolyl-O-phosphono-L-tyrosyl-L-leucyl-L-lysyl-L-threonyl- (9CI) (CA INDEX NAME)

NTE modified

SEQ 1 PYLKTK

Absolute stereochemistry.



RN 286465-39-2 HCAPLUS
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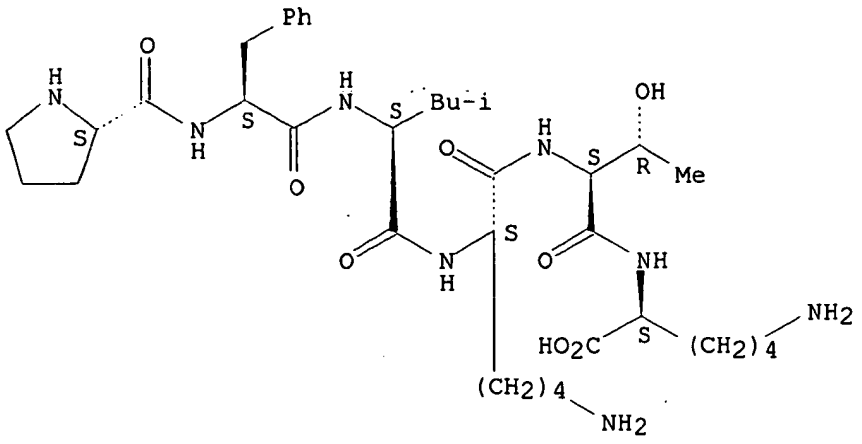
SEQ 1 PFLKTK

Absolute stereochemistry.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